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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,807	07/17/2003	Arthur M.P. Doweyko	D0250 NP	1455

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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	**PAPER NUMBER**
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/20/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,807	DOWEYKO ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed, Ph. D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-27 and 29-39* is/are pending in the application.

4a) Of the above claim(s) *2,3,11-15,17-26 and 30-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-10,16,27 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/31/04;9/28/05;& 10/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group I, claims 1, 5-10, 16, 27, and 29, directed to a method of evaluating compounds that binds to glucocorticoid receptor (GR) in the reply filed on October 26, 2006 is acknowledged.

The application has been amended as requested in the communication filed October 26, 2006. Accordingly, claim 4 has been canceled.

Claims 1, 5-10, 16, 27, and 29 are under consideration in this Office action.

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.C

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

The drawings are objected to under 37 CFR 1.83(a) because they fail to show the structures (Figures 3 and 7) as described in the specification. In particular, the color photographs are too dark that many of the details in the structure can't bee seen in black and white reproduction. Applicant may wish to consider the color scheme in the photograph so that reproduction in black and white show sufficient details of the structure intended to be shown. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement-drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The disclosure is objected to because of the following informalities: The reference to an attorney docket number in the paragraph bridging pages 75 and 76 page 76 is not a proper reference.

Appropriate correction is required.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s). In particular, 37 CFR 1.821, which states:

> (d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Tables I-V represent linear amino acid sequence disclosures, and therefore, each Table need a heading identifying the protein name and its SEQ ID NO: 1. The amino acid sequences at page 97 should be identified by a sequence identification number. In addition, each time in the specification and the claims, any reference to a specific protein, which is listed in the sequence listing, said reference should be accompanied by a sequence identification number. Perfecting the compliance with the sequence rule is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 22, lines 12 and 23, and page 96, line12. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1 and 5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Consideration of the "Computer-Related Inventions" section of the MPEP at section 2106, Part IV, subpart B, has revealed that the instant claims are directed to non-statutory subject matter without requiring performance of a result outside of a computer or representing some type of physical transformation which is concrete or tangible. Thus, the manipulation of data or conversion of data, in this case restriction fragment patterns is the claimed subject matter without any physical transformation

outside of a computer or representation thereof. It is noted that the last 2 lines of instant claim 1 cites analyzing structural and chemical features complementarity between said chemical entity and all or any part of said GR site II, but without requiring any outside of the computer output. For example, it is well known that a software program may output results to a computer file and not display it, for example, outside of the computer. Similarly, the design step in claim 5 is a calculation step, which is automated and generate an in computer file. The above instant claims also lack statutory subject matter due to being directed to nonfunctional descriptive material since the claims lack performance or control of a physical transformation. The presence of such nonfunctional descriptive material on a computer medium or in a computer system does not prevent this rejection because such nonfunctional descriptive material lacks the implementation of physical functionality regarding such computer elements. Additionally, applicant(s) may wish to argue that the methods are directed to a practical invention. Consideration of the MPEP at section 2106, Part IV, subpart B, sub-subpart 2, reveals that such a practical invention type requires the production of a useful, concrete, and tangible result which is reasonably interpreted as at least some physicality of result or representation thereof as required for statutory subject matter. Methods *per se* as instantly claimed subject matter are reasonably deemed a manipulation of data for such methods, without any physicality, that is, concrete or tangible, requirement. It is noted that the practical invention requirement is directed to a required combination of a useful, concrete, and tangible result, which supports this rejection if only one or more of these criteria fail to be met in the claimed subject matter. It is noted that instantly pending claims, which are reasonably interpreted as requiring physical transformation(s) or representation thereof are not rejected herein under.

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 5-10, 16, 27, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) The phrase "any part of the cavity" in claims 1, 6, and 29, "any part of" in claim 5, renders the claim indefinite because the resulting claim does not define the metes and bound of the claimed invention. Any part of the cavity reads on one atom. It is not possible to dock a chemical entity to one atom.

(b) The amino acid residues numbers in claims 1, 5, 6, 27, and 29 do not match the amino acid sequence of SEQ ID NO: 13 as well as those in Figure 2, which render the claims indefinite and confusing.

SEQ ID NO: 13 is 255 amino acid residues and the numbers in the claims are from residues 537-667. The amino acid of SEQ ID NO: 13 is that of MR in Figure 2, which begins with residue 731 and end with residue 984. For examination purposes only, it is assumed that the amino acid residues refers to amino acid sequence of the full-length GR protein from which SEQ ID NO: 12 is a fragment thereof.

(c) The phrase "human GR; rat GR; mouse RG; .....and m'az monkey RG" in claim 16 renders the claim indefinite because the resulting claim does not defines the metes and bound of the claimed invention. The phrase refers to amino acid sequences disclosed in the sequence listing, and therefore; these sequences should be accompanied by a sequence identification number.

(d) Claims 7-10 are included in with these rejection because the claims are dependent on a rejected claim and do not cure its deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-10, 16, 27, and 29 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US patent 6,965,850 ('850).

The '850 patent teaches the three-dimensional structure of the thyroid receptor (TR) and its co-activator binding site (Site II). See the abstract. Figure 19 teaches the homologues structure elements that define the co-activators binding sites of various nuclear receptors including the human GR. Also, the '850 patent teaches methods of identifying agonists and antagonist for said receptors using the atomic coordinates for the co-activator binding site as well as the software packages used to carry out the method and assay methods. See column 7 line 34 through column 13, line 49 and example 3, column 19. In addition, the '850 patent claims a method of identifying compound that modulate the activity of said receptors including GR using the atomic coordinates for the site II amino residues. See claims 1 and 18.

The method taught and claimed in the '850 patent appears to be identical to that of the instant application. The co-activator binding site of the '850 patent is defined by amino acid residues from helices 3, 4, 5, 6, and 12, which are involved in the formation of site II of the instant application. See compare Figure 19 of the patent to Figure 3 of the instant application. Residues 570-577 and 598-600 define the site II in the application and the patent.

These rejections are being made under 35 U.S.C. 102(b) and 35 U.S.C. 103 because it is not possible for the Examiner to physically compare the site II of the instant application and that of the patent. Applicant bears the burden of providing evidence, which distinguishes the claimed method of the instant application and that disclosed in the '850 patent. A preferred means of providing this evidence is for applicant to submit a side-by-side comparison between the site of the application and that of the patent which demonstrates any significant differences between the co-activator site in the '850 patent and site II of the instant application and that the sites of the instant application is unobvious in view of the site disclosed in the '850 patent. *In re Best, Bolton, and Shaw* 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald, Sanders and Bagheri* 205 USPQ 594 (CCPA 1980).

Claims 1, 5-10, 16, 27, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/52050 ('050, IDS reference AM filed 9/28/05) in view of US patent 5,856,116 ('116, IDS reference 1A).

The '050 patent document teaches methods of homology modeling of the glucocorticoid receptor (GR) using the three-dimensional structure determined by X-ray crystallography of two different receptor and the computer software package named the "MODELER". See the abstract, pages 12-18. The atomic coordinates for the modeled structures are reported in Figures 12 and 13. Also, it teaches a binding assay method and methods of optimizing chemical structures to bind to the GR

receptor using the modeled structured as well as *de novo* drug design using software packages such as LUDI and LEAPFROG. See page 6 the fourth paragraph, page 11 last paragraph and pages 14-18. Also, the '050 patent document teach that the GR agonists are useful for treatment of inflammation and immunosuppressive therapy, whereas the antagonists are expected to be useful for the treatment of hypertension, diabetes, obesity, glaucoma, depression, AIDS, and wound healing. See pages 6, third paragraph.

The '116 patent is relied on to demonstrate the state of the art at the time of invention. In particular, it teaches that computers and software packages such as CHARMm, AMBER, GRAM, DUCK are AUTODUCK are commercially available.

The '050 patent document provide one of ordinary skill in the art with motivation to identify potential inhibitor for GR as they teach the agonist and antagonist can be used for the treatment of various known human diseases such as inflammation and diabetes. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to develop a method of identifying potential agonist or antagonists. Thus, it would have been obvious to one of ordinary skill in the art to use a commercially available computer equipped with a software package such as GRAM, DUCK, QUANTA, and AUTODUCK to fit a model structure of a potential inhibitor to the three-dimensional model taught in the '050 patent document. The only difference between the cited prior above and the claimed invention are the atomic coordinates of the site II ligand-binding site, which is an algorithm. Data, which are fed into known algorithm such as QUANTA whose purpose is to compare or modify those data using series of processing steps, do not impose a change in processing steps and are thus nonfunctional descriptive material. A method used for its known purpose to compare data sets does not become non-obvious merely because a new data becomes available for analysis. Nonfunctional descriptive material cannot render non-obvious an invention that has otherwise been obvious. Thus, the atomic coordinates for the amino acids for site II can't render a known method for identifying agonists and antagonists novel or non-obvious (claims 1 and 5). It would have been further obvious to the ordinary skilled artisan to synthesize the potential agonist or antagonist and contacting it with the GR receptor to identify its binding characteristics as taught in '050 patent (claims 6-10, 16, and 27).

Claims 1, 5-10, 16, 27, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2005/0181362 ('362).

The '362 document is qualified prior art under 35 USC 102(e), which is a pre-grant publication of the national stage application US 10/484,061 filed under 35 USC 371 of PCT/US02/22648 (IDS reference: WO 03/015692 A2), filed July 17, 2002, which claim priority to US provisional application 60/305,902, filed July 17, 2001. The provisional application is fully enabling the teaching below. The '362 document teaches the crystallization of the complex of GR ligand binding with two ligand and the

determination of three-dimensional structure by the X-ray diffraction method. See examples 6-8 at page 38 and Table 4, pages 41-106. Also, it teaches that glucocorticoids are used for the treatment of many diseases such as inflammation, connective tissue diseases, rheumatoid arthritis and various kinds of cancers such as leukemia, lymphomas, and breast cancer; and that glucocorticoids exert their effects after binding to their receptor. See page 2, paragraphs 7-9. In addition, it teaches methods of identifying compounds that modulate the activity of the GR receptor, and the soft ware package required for the identifying, design, and modifying modulator of activity and their commercial source as well as a method of measuring the binding of the modulator to GR ligand binding domain. See pages 20-23 and example 5 at page 37. This rejection is made under 35 USC 103 because the reference does not identify GR site II.

The '362 patent document provide one of ordinary skill in the art with motivation to identify potential inhibitor for GR as they teach the agonist and antagonist can be used for the treatment of various known human diseases. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to develop a method of identifying potential agonist or antagonists and use a commercially available computer equipped with a software package such as GRAM, DUCK, QUANTA, and AUTODUCK document to fit a model structure of a potential inhibitor to the three-dimensional model taught in the '362 patent document as taught in the '362 document. The only difference between the cited prior above and the claimed invention are the site II ligand-binding site, which is an algorithm. Data, which are fed into known algorithm such as QUANTA whose purpose is to compare or modify those data using series of processing steps, do not impose a change in processing steps and are thus nonfunctional descriptive material. A method used for its known purpose to compare data sets does not become non-obvious merely because a new data becomes available for analysis. Nonfunctional descriptive material cannot render non-obvious an invention that has otherwise been obvious. Thus, the atomic coordinates for the amino acids for site II can't render a known method for identifying agonists and antagonists novel or non-obvious (claims 1 and 5). It would have been further obvious to the ordinary skilled artisan to synthesize the potential agonist or antagonist and contacting it with the GR receptor to identify its binding characteristics as taught in the '362 document (claims 6-10, 16, and 27).

Claims 1, 5-10, 16, 27, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2005/0181362 ('362) in view of 6,965,850 ('850, Baxter *et al.*).

The teaching of the '362 patent document and the '850 patent are summarized above.

The '850 patent provides one of ordinary skill in the art with a motivation to identify modulator of the GR activity by utilizing the atomic coordinates of the co-activator binding site. While the '850 patent teach a modeled structure for the binding

site of the co-activator, one of ordinary skill in the art would have been motivated tc identify the co-activator binding site in the crystallographically determined structure taught in the '362 patent document because it is the more accurate and experimentally determined structure. Thus, it would have been obvious at the time of invention to one of ordinary skill in the art to use the structure taught in the '362 patent to identify the co-activator binding site, which is modeled and suggested in the '850 patent. Once the ordinary skill in the art identify the amino acid residue of the GR involved in binding the co-activator, he/she would have used the atomic coordinates of said residues to design, modify, or identify compounds that bind to said co-activator binding site (claims 1) and assay for their binding activity disclosed in both the '362 document or the '850 patent (claims 5-10, 16, 27, and 29). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934.. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner
Art Unit 1656